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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/674,581	TSUTSUI ET AL.	
	Examiner	Art Unit	
	Bruce D. Hissong, Ph.D.	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 July 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7,9,13,15,19,21-27 and 31-44* is/are pending in the application.

4a) Of the above claim(s) *21-27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7, 9, 13, 15, 19, 31-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Formal Matters

1. Applicants' response to the office action mailed on 3/13/2008, including arguments/remarks and amended claims, was received on 7/9/2008 and has been entered into the record.

2. In the response received on 7/9/2008, the Applicants added new claims 40-44. Claims 7, 9, 13, 15, 19, 21-27, and 31-44 are currently pending. Claims 21-27 are withdrawn as non-elected subject matter, and claims 7, 9, 13, 15, 19, and 31-44 are the subject of this office action.

Claim Objections

1. As currently written, claim 7 is a product claim. However, certain limitations of the claim suggest method steps (i.e. mucosal administration of the claimed adjuvant at the same time as a peptide/protein antigen). It is suggested to amend the claims to recite "A mucosal adjuvant comprising a natural interferon-α as the active ingredient, wherein said mucosal adjuvant induces both vaccine antigen-specific antibody in the blood and vaccine antigen-specific antibody secreted at the mucosal surface when mucosal administration of said adjuvant is performed at the same time as administration of a vaccine antigen" or something similar. A similar situation exists for claim 13, and a similar amendment is suggested.

2. The Examiner suggests amending the phrase "at the same time as a vaccine antigen" in claim 7 to "at the same time as administration of a vaccine antigen".

3. The Examiner suggests amending claims 9 and 15 to recite "wherein the amount of the interferon-α is 0.5 to 5,000,000 IU".

4. The Examiner suggests amending claim 44 to recite "a mucoadhesive microsphere".

Rejections Maintained

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

1. Claims 7, 9, 13, 15, 19, and 31-39 *remain rejected*, and new claim 41 is also rejected under 35 USC § 103(a) as being obvious in view of Staats *et al* (WO 00/20028) in view of Takasu (*Kurume Med J.*, 2001, Vol 48, p. 171-174) as set forth on pages 3-5 of the office action mailed on 3/13/2008.

The claims of the instant invention are drawn to a mucosal vaccine adjuvant comprised of a natural IFN-α, wherein nasal mucosal administration of said mucosal adjuvant and a protein/peptide vaccine antigen induces both vaccine antigen-specific antibody in blood and vaccine antigen-specific antibody secreted at the mucosal surface. The claims are also drawn to a combined product of a vaccine antigen and mucosal adjuvant comprised of a vaccine antigen and IFN-α, wherein the vaccine antigen is a protein or peptide antigen, the IFN-α is natural IFN-α, and wherein said nasal mucosal administration of said mucosal adjuvant/vaccine antigen induces both vaccine antigen-specific antibody in blood and vaccine antigen-specific antibody secreted at the mucosal surface. The claims further recite specific amounts of IFN-α, and locations for inducting of vaccine-specific antibody and specific types of antibodies. New claims 40-41 recite specific percentages of vaccine antigen and IFN-α.

Staats teaches a method of eliciting an immune response by administration of a vaccine antigen and an adjuvant (see abstract, and claim 1). Staats teaches that the vaccine antigen can be either protein or peptide antigens, including protein/peptide antigens from a number of pathogenic organisms (see p. 21, line 11 – p. 23, line 2). Staats also teaches that various cytokines can be used as adjuvants (see p. 14, line 19 – p. 15, line 2, and claims 5-6). Furthermore, Staats teaches mucosal administration of the vaccine-adjuvant combination (claim 17), and also teaches that the vaccine-adjuvant induces both systemic (claim 22) and mucosal (claim 25) immune responses. Finally, by teaching that the vaccine and adjuvant are included together as a composition, Staats teach that the vaccine antigen and the adjuvant are administered at the same time and by the same route of administration. However, Staats is silent regarding the use of IFN-α as the adjuvant for any antigen-adjuvant combination or composition.

Takasu teaches that IFN-α is a potent adjuvant for increasing the immune response to various vaccine antigens. Specifically, Takasu discloses that co-administration of IFN-α with influenza virus peptide increased the cytotoxic T lymphocyte (CTL) response to the influenza virus peptide compared to vaccination with the influenza virus peptide alone (see p. 172-174, Figures 1-3).

In the response received on 7/9/2008, the Applicants argue that Staats does not teach a mucosal adjuvant comprising IFN-α, and instead provides a laundry list of other cytokines with different biological activities. The Applicants also argue that Takasu teaches away from the present invention because it teaches continuous administration of peptide antigen via an osmotic pump and injection of IFN-α, rather than nasal administration of peptide antigen and IFN-α at the same time, as currently claimed. Therefore, because the routes of administration of Staats are different from the use and methods of Takasu, there would be no motivation to combine the two references. Furthermore, the Applicants argue that any *prima facie* case of obviousness is rebutted by the declaration submitted by Mr. Yuuki Tsutsui showing unexpectedly improved properties of the instant invention which are not present in the prior art. Specifically, the Applicants argue that the Tsutsui declaration shows that mucosal administration of IFN-α and the antigen ovalbumin (OVA) produced higher levels of both circulating OVA-specific IgG antibodies and mucosa OVA-specific IgA antibodies compared to administration of OVA with either IFN-β or cholera toxic B. In view of these unexpectedly improved results, the Applicants argue that the claims of the instant invention cannot be held as obvious in view of any combination of art.

These arguments have been fully considered and are not persuasive. Staats teaches that mucosal administration of a vaccine antigen results in both systemic and mucosal immune responses, while Takasu teaches that IFN-α is a potent vaccine adjuvant. Although the route of administration in Takasu differs from that of Staats, one of ordinary skill in the art would be motivated to adapt the IFN-α adjuvant to the mucosally-administered vaccine/adjuvant combination of Staats because the skilled artisan would expect that the adjuvant properties of IFN-α would enhance the systemic and mucosal immunity provided by the method of Staats. Therefore, it would be prima facie obvious to combine the teachings of Staats and Takasu to create a mucosal vaccine adjuvant comprising IFN-α.

Regarding Applicants' assertion that the vaccine adjuvant of the instant invention provides unexpectedly improved results, as set forth in the declaration by inventor Tsutui, it is noted that although a composition comprising OVA and IFN-α induced higher levels of systemic and mucosal OVA-specific antibodies compared to IFN-β or CTB as adjuvants, it is noted that these results would not be unexpected because Takasu teaches that IFN-α is a potent adjuvant. Thus, one of ordinary skill in the art would

expect such results because the skilled artisan would know that the function of an adjuvant is to increase the immune response to a given antigen, and Takasu teaches that IFN-α is a potent adjuvant.

Finally, although neither Staats nor Takasu specifically teach the cited percentages of IFN-a, it would be obvious to one of ordinary skill in the art to optimize the dosage/percentage of each in order to create a composition which most effectively induces vaccine antigen-specific antibodies. MPEP 2144.05 states:

"[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 454, 105 USPQ 223, 235, (CCPA 1955).

In the instant case, the general conditions of a vaccine adjuvant comprising IFN-α is obvious in view of Staats and Takasu, as set forth *supra*. Therefore, one of ordinary skill in the art would have the motivation to optimize the dose/percentage of IFN-α in the claimed adjuvant. It is also noted that claim 40 has not been included in this rejection because the language of claim 19 only specifies that the mucosal adjuvant comprise IFN-α. Although the claim recites a vaccine antigen comprising a protein or peptide antigen, the language of the claim does not require the claimed adjuvant to comprise a vaccine antigen. However, if the claim 19 did in fact require the claimed adjuvant to comprise IFN-α and a vaccine adjuvant, then dependent claim 40 would also be rejected as obvious because it would be obvious to optimize the concentration of said vaccine antigen for the reasons stated *supra*.

2. Claims 7, 9, 13, 15, 19, and 31-39 *remain rejected*, and new claim 41 is also rejected under 35 USC § 103(a) as being obvious in view of Foster *et al* (US 6,436,391) in view of Tovey (US 6,361,769) as set forth on pages 5-6 of the office action mailed on 3/13/2008.

The subject matter of the claims of the instant invention is discussed *supra*. Foster teaches the use of IFN-α as a vaccine adjuvant to increase B lymphocyte proliferation, and thus increase the effectiveness of vaccines (column 1, lines 52-56), and specifically recites co-administration of a vaccine with IFN-α, or alternatively, a composition comprised of IFN-α and a vaccine (column 1, lines 61-65). Foster is silent regarding mucosal administration of an IFN-α vaccine-adjuvant composition, and is also silent regarding specific amounts or doses of IFN-α.

Tovey teaches a method of stimulating host immunity by oromucosal administration of IFN-α (column 2, line 32 – column 3, line 28). Tovey discloses specific doses of IFN-α that can be oromucosally administered (column 3, line 15-20), and also teaches that IFN-α can be administered as an

adjunct to other therapy (column 3, lines 21-22), and specifically mentions previous studies in which IFNs where orally administered to enhance the efficiency of vaccines (column 1, lines 61-66).

In the response received on 7/9/2008, the Applicants argue that Foster teaches an adjuvant for a vaccine comprising IFN-α_8 and/or IFN-α_{14}, but does not teach a vaccine adjuvant comprising a natural IFN-α. The Applicants also argue that Tovey does not teach or suggest a mucosal adjuvant comprising IFN-α and a peptide or protein antigen that would elicit a systemic immune response as well as a mucosal response. Furthermore, the Applicants argue that any *prima facie* case of obviousness is rebutted by the declaration submitted by Mr. Yuuki Tsutsui showing unexpectedly improved properties of the instant invention which are not present in the prior art. Specifically, the Applicants argue that the Tsutsui declaration shows that mucosal administration of IFN-α and the antigen ovalbumin (OVA) produced higher levels of both circulating OVA-specific IgG antibodies and mucosa OVA-specific IgA antibodies compared to administration of OVA with either IFN-β or cholera toxic B. In view of these unexpectedly improved results, the Applicants argue that the claims of the instant invention cannot be held as obvious in view of any combination of art.

These arguments have been fully considered and are not persuasive. As acknowledged by the Applicants on page 9 of the response received on 7/9/2008, Foster discloses an adjuvant for a vaccine comprising IFN-α_8 and/or IFN-α_{14}. The Applicants argue that Foster does not disclose a vaccine adjuvant comprising "natural" IFN-α; however, it is well-known in the art that both IFN-α_8 and/or IFN-α_{14} are naturally-occurring human IFN-α gene products (see Pestka, cited in the previous office action), and in the absence of a preferred definition of "natural" IFN-α in the instant specification, both IFN-α_8 and/or IFN-α_{14} could be considered to be "natural" IFN-α. Because Tovey teaches that oromucosal administration of IFN-a is effective in modulating immunity and is useful as an adjunct to other therapy, one of ordinary skill in the art would have the motivation to administer the IFN-a vaccine adjuvant of Foster via the oromucosal route taught by Tovey. It is noted that Pestka is not being used as a new grounds of rejection, but to point out what was well-known in the art regarding "natural" IFNs.

Regarding Applicants' assertion that the vaccine adjuvant of the instant invention provides unexpectedly improved results, as set forth in the declaration by inventor Tsutui, it is noted that although a composition comprising OVA and IFN-α induced higher levels of systemic and mucosal OVA-specific antibodies compared to IFN-β or CTB as adjuvants, it is noted that these results would not be unexpected because Takasu teaches that IFN-α is a potent adjuvant. Thus, one of ordinary skill in the art would

expect such results because the skilled artisan would know that the function of an adjuvant is to increase the immune response to a given antigen, and Foster teaches that IFN-α is a potent adjuvant.

Finally, although neither Foster nor Tovey specifically teach the cited percentages of IFN-α, it would be obvious to one of ordinary skill in the art to optimize the dosage/percentage of each in order to create a composition which most effectively induces vaccine antigen-specific antibodies. MPEP 2144.05 states:

"[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 454, 105 USPQ 223, 235, (CCPA 1955).

In the instant case, the general conditions of a vaccine adjuvant comprising IFN-α is obvious in view of Foster and Tovey, as set forth *supra*. Therefore, one of ordinary skill in the art would have the motivation to optimize the dose/percentage of IFN-α in the claimed adjuvant. It is also noted that claim 40 has not been included in this rejection because the language of claim 19 only specifies that the mucosal adjuvant comprise IFN-α. Although the claim recites a vaccine antigen comprising a protein or peptide antigen, the language of the claim does not require the claimed adjuvant to comprise a vaccine antigen. However, if the claim 19 did in fact require the claimed adjuvant to comprise IFN-α and a vaccine adjuvant, then dependent claim 40 would also be rejected as obvious because it would be obvious to optimize the concentration of said vaccine antigen for the reasons stated *supra*.

New Grounds of Rejection/Rejections Necessitated by Amendment

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 9 and 13 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966). In the instant case claims 9 and 15 depend from claims 7 and 13, respectively, which are

claims to compositions, rather than claims to methods. As such, they cannot recite any steps involved in any method/process for the "use" of IFN-α.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

1. Claims 9 and 15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 9 and 15 provide for the use of IFN-α, but, since the claims do not set forth any steps involved in the method/process, it is unclear what method/process Applicants are intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced. In the instant case claims 9 and 15 depend from claims 7 and 13, respectively, which are claims to compositions, rather than claims to methods. As such, they cannot recite any steps involved in any method/process, and therefore it is not clear how the recited IFN-α is to be "used".

2. Claim 40 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claim is drawn to the ratio of vaccine antigen in the claimed mucosal adjuvant is 0.01 to 55% w/w of the entire composition. However, claim 19, from which claim 40 depends, recites a mucosal adjuvant comprising IFN-α, and does not specify that the claimed mucosal adjuvant comprise a vaccine antigen. Thus, it is not clear how the mucosal adjuvant of claim 19 can be comprised of a certain percentage of vaccine antigen when the claim does not specify that the mucosal adjuvant actually comprise a vaccine antigen.

3. Claims 40-41 recite the limitation "the entire composition" in claim 19. There is insufficient antecedent basis for this limitation in the claim.

4. Claim 43 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claim recites the undefined acronym PLGA. Acronyms should be defined upon their first use in a claim, and the presence of an undefined acronym renders the claim indefinite.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

1. Claims 7, 9, 13, 15, 19, and 31-39 are rejected under 35 U.S.C. 102(b) as being anticipated by Takasu.(*Kurume Med J.*, 2001, Vol 48, p. 171-174 – cited previously). The subject matter of the claims of the instant invention is discussed supra. Furthermore, it is noted that independent claims 7, 13, and 19 are product claims, rather than method claims, and are drawn to a mucosal adjuvant comprising a natural IFN-α, or a combined product of a vaccine antigen and mucosal adjuvant, wherein said combined product comprises a natural IFN-α.

Takasu teaches a composition comprising IFN-α and a peptide antigen derived from influenza virus (see p. 172, 2nd column - 1st paragraph of "Results"), and administration of this IFN-a/peptide composition to mice. Takasu discloses that the IFN-α is murine IFN-α produced by infecting cells with a virus, and thus the produced IFN-α could be considered a "natural" IFN-α, especially in the absence of a preferred definition in the specification. Because claims 7 and 19 only require that the claimed mucosal adjuvant comprise a natural IFN-α, Takasu meets the limitation of claims 7 and 19. Likewise, even though the preamble of claim 13 specifies a "combined product of vaccine antigen and mucosal adjuvant", it also only requires the combined product to comprise IFN-α, and therefore the limitations of claim 13 are also met. Takasu also teaches that the IFN-α was present in a concentration of 1×10^5 U, which meets the limitations of claims 9 and 15.

Furthermore, Takasu teaches that the IFN-α acted as a potent adjuvant for increasing the immune response to a vaccine antigen derived from influenza virus (see Fig 1). Although Takasu does not

specifically teach induction of influenza peptide-specific IgG antibody in the blood and IgA antibody at the mucosal surface, such as the gastrointestinal surface, it is noted that the IFN-α used in Takasu is administered at the same time as a peptide antigen (see Fig 1), is a "natural" IFN-α, and that independent claims only require that the claimed mucosal adjuvant comprise IFN-α. Thus, the IFN-α composition of Takasu would be expected to function as a mucosal adjuvant for the influenza peptide, and in the absence of evidence to the contrary, would be expected to inherently be capable of inducing vaccine antigen-specific IgG antibody in the blood and IgA antibody at the mucosal surfaces. It is noted that the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer. *Atlas Powder Co. v Ireco Inc.* 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). Furthermore, case law has established that a compound and all of its properties are inseparable, as are its processes and yields (*In re Papesch*, 315 F.2d 381, 137 USPQ 43 (CCPA 1963)). Therefore, because the claims only require that the claimed mucosal adjuvant comprise a "natural IFN-α", and Takasu teaches a composition comprising natural IFN-α, as well as a vaccine antigen, the composition of Takasu would inherently meet the limitations of the instant claims.

2. Claims 7, 9, 13, 15, 19, and 31-39 are rejected under 35 U.S.C. 102(e) as being anticipated by Tovey *et al* (US 6,361,769 – cited previously).

The subject matter of the instant invention is described *supra*. Tovey teaches a composition comprising natural murine IFN-α at 4 x 10^6 IU/ml (column 6, lines 19-31), and oromucosal administration of this IFN-a (see Examples 1-3). In absence of evidence to the contrary, this composition of natural IFN-α could be considered to be a mucosal adjuvant because the claims of the instant invention only require that a mucosal adjuvant comprise natural IFN-α. Furthermore, because this composition is the same as that which is currently claimed, the composition of Tovey would be expected, in the absence of evidence to the contrary, to inherently be capable of inducing vaccine-antigen dependent IgG antibody in the blood and IgA antibody at mucosal surfaces. As set forth above, the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer. *Atlas Powder Co. v Ireco Inc.* 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). Furthermore, case law has established that a compound and all of its properties are inseparable, as are its processes and yields (*In re Papesch*, 315 F.2d 381, 137 USPQ 43 (CCPA 1963)). In the instant case, the composition of Tovey does

not differ from that which is currently claimed, and therefore the composition of Tovey meets the limitations of claims 7, 9, 13, 15, 19, and 31-39 of the instant invention.

3. Claims 7, 9, 13, 15, 19, and 31-39 are rejected under 35 U.S.C. 102(e) as being anticipated by Foster *et al* (US 6,436,391 – cited previously).

The subject matter of the instant invention is discussed *supra*. Foster discloses a vaccine adjuvant comprising IFN-α (column 1, lines 57-65; claims 1-2). Specifically, Foster teaches an adjuvant composition comprising IFN-α_8 and/or IFN-α_{14}. It is noted that the instant specification does not provide a preferred definition for "natural" IFN-α, and it is well-known in the art that these IFN-a subtypes are naturally occurring human IFN-α polypeptides (see Pestka - cited in previous office action). In absence of evidence to the contrary, this composition could be considered to comprise "natural" IFN-α, and could also be considered to be a mucosal adjuvant because the claims of the instant invention only require that a mucosal adjuvant comprise natural IFN-α. Furthermore, because this composition is the same as that which is currently claimed, the composition of Foster would be expected, in the absence of evidence to the contrary, to inherently be capable of inducing vaccine-antigen dependent IgG antibody in the blood and IgA antibody at mucosal surfaces. As set forth above, the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer. *Atlas Powder Co. v Ireco Inc.* 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). Furthermore, case law has established that a compound and all of its properties are inseparable, as are its processes and yields (*In re Papesch*, 315 F.2d 381, 137 USPQ 43 (CCPA 1963)). In the instant case, the composition of Foster does not differ from that which is currently claimed, and therefore the composition of Foster meets the limitations of claims 7, 9, 13, 15, 19, and 31-39 of the instant invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

1. Claim 41 is rejected under 35 U.S.C. 103(a) as being unpatentable over either Takasu or Tovey *et al* or Foster *et al*.

The subject matter of the instant application and the disclosures of Takasu, Tovey, and Foster are discussed *supra*. Claim 41 is further drawn to the mucosal adjuvant of claim 19, wherein the ratio of IFN-α is 0.01 to 5% w/w of the entire composition. Although neither Takasu, Tovey, nor Foster specifically recites the claimed ratio/percentages of IFN-α, they teach the therapeutic utility of IFN-α compositions as vaccine adjuvants or for stimulating immunity. Therefore, one of ordinary skill in the art would be motivated to optimize the dosage/percentage of IFN-α in the compositions of Takasu, Tovey, and/or Foster in order to create an adjuvant which most effectively induces vaccine antigen-specific antibodies or stimulates immunity. MPEP 2144.05 states:

"[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 454, 105 USPQ 223, 235, (CCPA 1955).

In the instant case, the general conditions of a composition comprising IFN-α is specifically taught by Takasu, Tovey, or Foster, as set forth *supra*. Therefore, one of ordinary skill in the art would have the motivation to optimize the dose/percentage of IFN-α in this composition.

2. Claims 42-44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Takasu in view of Kawashima *et al* (*Pharm. Dev. Tech*., 2000, Vol. 5(1), p. 77-85).

The subject matter of the instant application is discussed *supra*. Claims 42-44 are further drawn to the mucosal adjuvant of claim 19, wherein said mucosal adjuvant is encapsulated in a member selected from the group consisting of a liposome, a nanosphere, a microsphere, a biodegradable carrier, and a mucoadhesive carrier, and specifically recites the biodegradable polymer PLGA and mucoadhesive microspheres and a mucoadhesive carrier.

As set forth *supra*, Takasu teaches a composition of IFN-α which functions as a potent vaccine adjuvant. Takasu is silent regarding encapsulation of this IFN-α composition in any liposome, nanosphere, microsphere, etc. However, Kawashima teaches that PLGA is a biocompatible and biodegradable carrier suitable for delivering numerous peptides/proteins (p. 78, 1st column, 2nd paragraph). Furthermore, Kawashima teaches modification of PLGA delivery systems in order to create mucoadhesive PLGA nonospheres. Specifically, Kawashima discloses PLGA nanospheres coated with a mucoadhesive polymer such as poly(acrylic acid), sodium alginate, and chitosan (see p. 78, 1st column, 3rd

paragraph; p. 79, 1st column, 2nd paragraph). Kawashima also shows that intragastric administration of these mucoadhesive PLGA nanospheres resulted in adhesion to the mucosal surface of the gut (Fig. 4).

Therefore, one of ordinary skill in the art, at the time the instant invention was conceived, would have been motivated to create a composition comprising IFN-α as an adjuvant and a mucoadhesive PLGA nanosphere of Kawashima for the purpose of more effective vaccination. The motivation to do so comes from Takasu, which teaches that IFN-α is a potent vaccine adjuvant, and Kawashima, which provides a compound for effective delivery of peptide/protein agents. Thus, one of ordinary skill in the art would know that encapsulation of the IFN-α of Takasu with the mucoadhesive PLGA of Kawashima would provide more efficient delivery of the IFN-α adjuvant.

3. Claims 42-44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tovey in view of Kawashima *et al* (*Pharm. Dev. Tech.*, 2000, Vol. 5(1), p. 77-85).

The subject matter of the instant application is discussed *supra*. Claims 42-44 are further drawn to the mucosal adjuvant of claim 19, wherein said mucosal adjuvant is encapsulated in a member selected from the group consisting of a liposome, a nanosphere, a microsphere, a biodegradable carrier, and a mucoadhesive carrier, and specifically recites the biodegradable polymer PLGA and mucoadhesive microspheres and a mucoadhesive carrier.

As set forth *supra*, Tovey teaches a composition of IFN-α which is immunostimulatory when administered via the oromucosal route. Tovey is silent regarding encapsulation of this IFN-α composition in any liposome, nanosphere, microsphere, etc. However, Kawashima teaches that PLGA is a biocompatible and biodegradable carrier suitable for delivering numerous peptides/proteins (p. 78, 1st column, 2nd paragraph). Furthermore, Kawashima teaches modification of PLGA delivery systems in order to create mucoadhesive PLGA nonospheres. Specifically, Kawashima discloses PLGA nanospheres coated with a mucoadhesive polymer such as poly(acrylic acid), sodium alginate, and chitosan (see p. 78, 1st column, 3rd paragraph; p. 79, 1st column, 2nd paragraph). Kawashima also shows that intragastric administration of these mucoadhesive PLGA nanospheres resulted in adhesion to the mucosal surface of the gut (Fig. 4).

Therefore, one of ordinary skill in the art, at the time the instant invention was conceived, would have been motivated to create a composition comprising IFN-α as an adjuvant and a mucoadhesive PLGA nanosphere of Kawashima for the purpose of more effective vaccination. The motivation to do so comes from Tovey, which shows that oromucosal administration IFN-α is effective in stimulating immunity, and Kawashima which provides a compound for effective delivery of peptide/protein agents.

Thus, one of ordinary skill in the art would know that encapsulation of the IFN-α of Tovey with the mucoadhesive PLGA of Kawashima would provide more efficient delivery of the oromucosally administered IFN-α.

Conclusion

No claim is allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bruce D. Hissong, Ph.D., whose telephone number is (571)272-3324. The examiner can normally be reached M-F from 8:30 am - 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, Ph.D., can be reached at (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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